

PATENT SPECIFICATION

NO DRAWINGS

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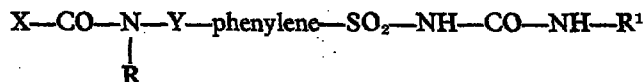
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COMPLETE SPECIFICATION

Benzenesulfonyl Ureas and process for their manufacture

We, FARBERWERKE HOECHST AKTIENGESSELLSCHAFT, Vormalis Meister Lucius & Brüning, a Company recognised by German Law, of 6230 Frankfurt (M)-Hoechst, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention provides benzenesulfonyl-ureas corresponding to the general formula



and physiologically tolerable salts of such compounds, wherein

R represents a lower alkyl or phenyl-lower-alkyl radical, or preferably a hydrogen atom;

R¹ represents

- (a) a cyclohexyl radical containing a methyl group and an alkoxy group containing 1 or 2 carbon atoms,
- (b) a chlorocyclohexyl group,
- (c) a spiro-(5,5)undecyl-(3) group of the formula



- (d) an exo-tricyclo-(3,2,1,0^{2,4}) octane group of the formula



- (e) a 4-methylcyclohexenyl group, or
- (f) a dimethyl- or 4,4-diethylcyclohexenyl group;

X represents

- (a) a phenyl radical, carrying in any desired positions the substituents Z and Z' which may be identical or different, in which

Z represents a hydrogen or halogen atom or a lower alkyl, lower alkenyl, lower alkoxy, lower alkenoxy, lower halogen-alkoxy, lower alkoxyalkoxy, phenyl-lower-alkoxy, phenyl-lower-alkyl, lower cycloalkoxy, phenyl, phenoxy, lower acyl, lower acyloxy or a benzoyl radical, or a trifluoromethyl, hydroxyl, —CN, or —NO₂ group,

- Z'** represents a hydrogen or halogen atom or a lower alkyl, lower alkoxy, lower alkoxyalkoxy or lower acyloxy radical or a hydroxyl group,
- (b) a naphthyl radical which may be mono- or di-substituted by a halogen atom or a lower alkyl or lower alkoxy radical or a hydroxyl group,
- (c) a tetrahydronaphthyl radical or an indanyl radical,
- (d) a thienyl radical which may be mono- or di-substituted by substituents selected from lower alkyl, phenyl-lower-alkyl, lower alkoxy, lower alkoxyalkoxy, lower alkenoxy, phenyl lower-alkoxy and aryl radicals and halogen atoms,
- (e) a tetra methylene-thienyl radical or a trimethylene-thienyl radical, the meaning of X mentioned under a) being preferred; and

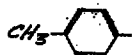
Y represents a hydrocarbon chain of 1—3 carbon atoms, preferably the grouping $-\text{CH}_2-\text{CH}_2-$, and wherein the phenylene group may be substituted by one or more substituents selected from halogen, lower alkyl or lower alkoxy.

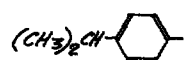
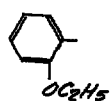
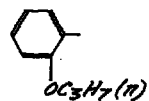
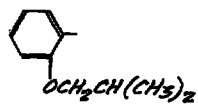
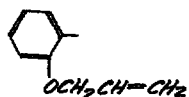
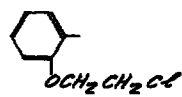
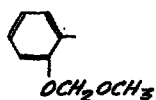
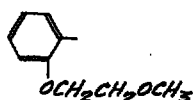
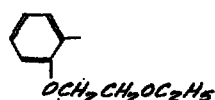
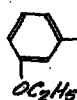
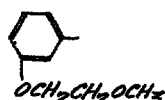
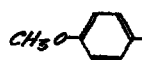
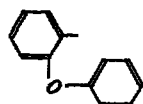
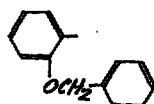
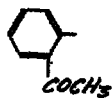
The compounds of the above general formula are new. These compounds and their physiologically tolerable salts exhibit hypoglycemic properties and are characterised by a long lasting hypoglycemic action.

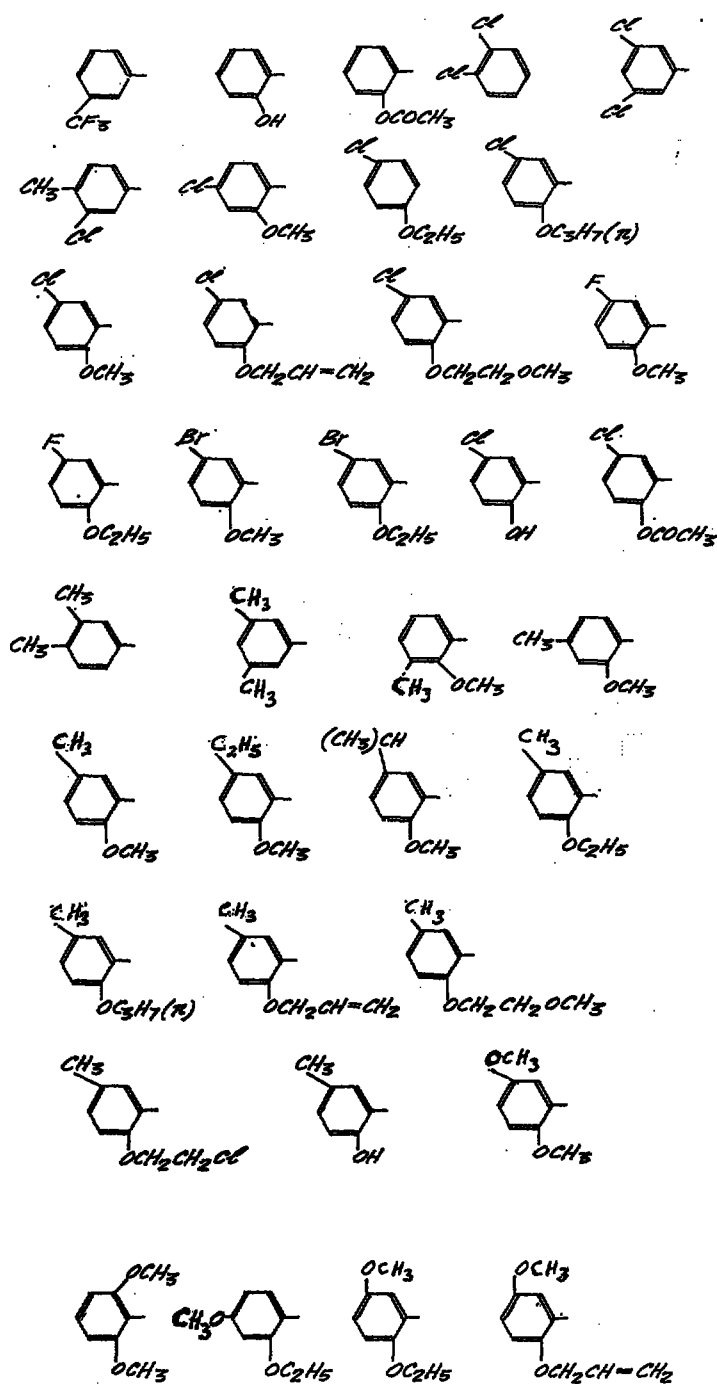
In the above in the following definitions and in the claims "lower" always means "containing 1 to 4 carbon atoms". The "lower acyl" radical (organic acid radical) containing up to 4 carbon atoms is preferably a straight-chained or branched alkanoyl radical of a corresponding length of chain.

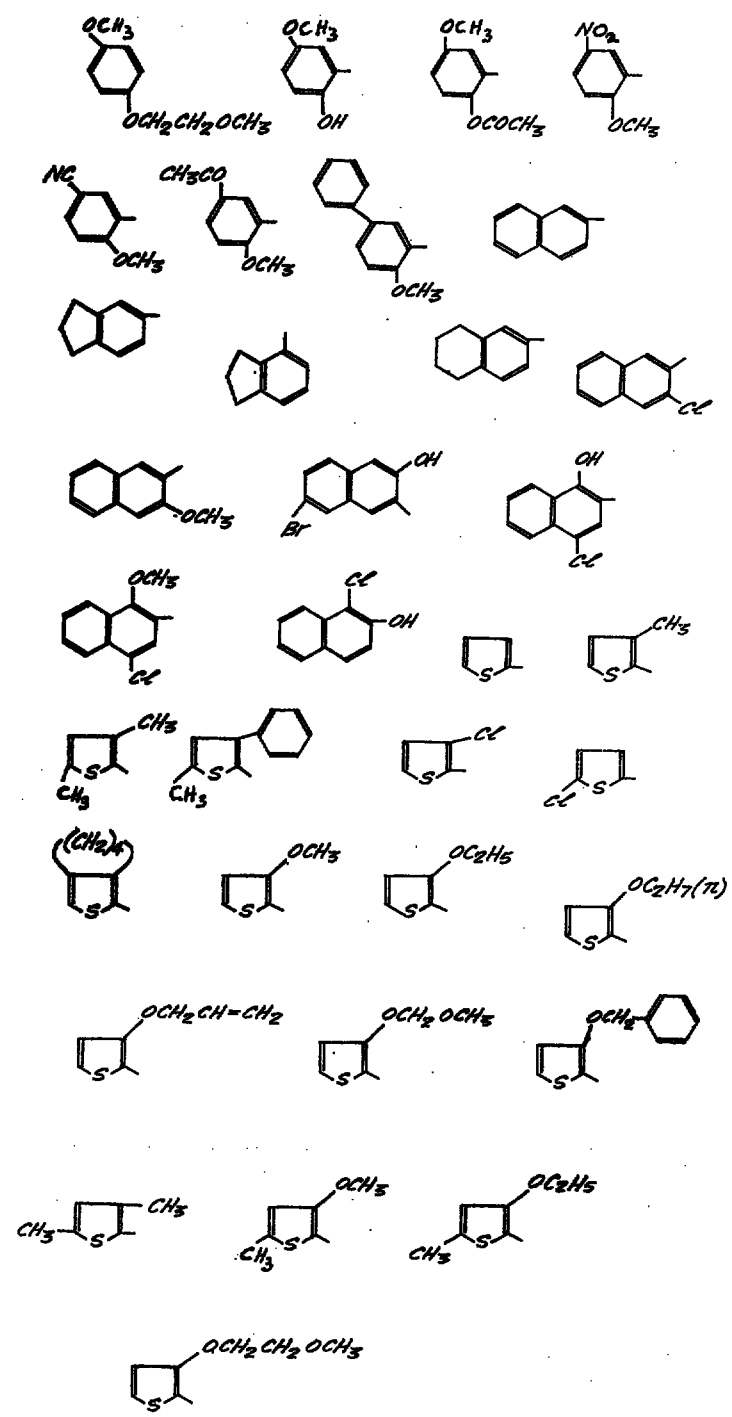
According to the above-mentioned definitions R may represent, for example, methyl, ethyl, propyl, butyl, benzyl, β -phenylethyl, compounds in which R represents hydrogen being preferred.

Ring systems representing the member X in the above-mentioned formula are, for example, the following:

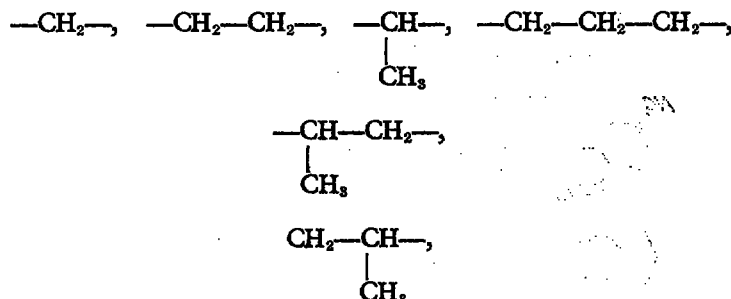








As examples for the bridge member Y which joins the benzene nucleus to the carbonamide group there are mentioned:



preferably those which separate the benzene nucleus from the carbonamide group by 2 carbon atoms.

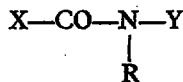
As R¹ the following radicals are mentioned:

2-, 3- or 4-chlorocyclohexyl, 3-methoxy-4-methyl-cyclohexyl, 3-ethoxy-4-methyl-cyclohexyl, 3-methyl-4-methoxy-cyclohexyl, 2-methyl-4-methoxy-cyclohexyl, 4-methyl-Δ³-cyclohexenyl.

The phenylene group mentioned in the formula by "phenylene" is preferably unsubstituted. It may, however, be mono- or poly-substituted by halogen, lower alkyl or lower alkoxy. It may carry the remaining parts of the molecule in ortho-, meta- or para-position to each other, the para-position being preferred.

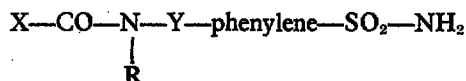
The present invention also relates to processes for the preparation of said benzene-sulfonyl-ureas wherein

- a) benzenesulfonyl-isocyanates, benzenesulfonyl-carbamic acid esters, benzenesulfonyl-thiocarbamic acid esters, benzenesulfonyl-carbamic acid halides or benzenesulfonyl-ureas, benzenesulfonyl-semicarbazides or benzenesulfonyl-semicarbazones substituted by the group



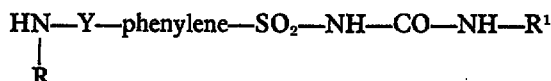
are reacted with R¹-substituted amines or, if desired, the salts thereof,

- b) benzenesulfonamides of the formula



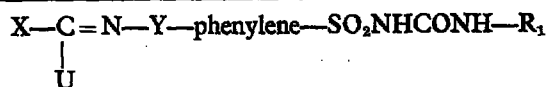
or their salts are reacted with R¹-substituted isocyanates, carbamic acid esters, thio-carbamic acid esters, carbamic acid halides or ureas,

- c) correspondingly substituted benzenesulfonyl-isourea ethers, benzenesulfonyl-isothio-urea ethers, benzene-sulfonyl-isourea esters, benzenesulfonyl-parabanic acids or benzenesulfonyl-haloformic acid amidines are hydrolyzed,
d) in correspondingly substituted benzenesulfonyl-thioureas the sulfur atom is exchanged for an oxygen atom,
e) to correspondingly substituted carbodiimides water is added,
f) corresponding benzenesulfonyl-ureas or benzenesulfonyl-ureas are oxidized,
g) in benzenesulfonyl-ureas of the formula

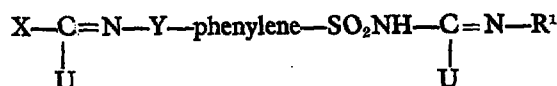


the radical X-CO- is introduced by acylation, if desired in several stages,

- h) correspondingly substituted benzenesulfonyl-halides are reacted with R¹-substituted ureas,
i) in correspondingly substituted thioamidoalkyl-benzene-sulfonyl-ureas or benzene-sulfonyl-thioureas the sulfur atom or the sulfur atoms are exchanged by an oxygen atom or oxygen atoms,
j) if R is H, compounds of the formula



or their parabanic acid derivatives or compounds of the formula



wherein U represents O-lower alkyl, S-lower alkyl or halogen (preferably chlorine) are saponified, or

k) in cases in which R^1 is not 4-methylcyclohexenyl, corresponding benzenesulfonyl-ureas containing in the molecule unsaturated bonds, are hydrogenated and the reaction products are treated with alkaline agents, if the formation of salts is desired.

According to the nature of the starting substances, in particular with regard to the member X, one or the other method mentioned above for the preparation of certain individual compounds corresponding to the general formula may be unsuitable in some cases, or, at least require measures for the protection of active groups. Such cases which do not occur very often can easily be recognized by the expert and there will be no difficulty in applying in these cases one or the other methods of synthesis described above.

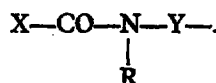
Instead of the benzenesulfonyl-isocyanates there can likewise be used reaction products of benzenesulfonyl-isocyanates with acid amides such, for example, as caprolactam or butyrolactam, furthermore with weakly basic amines such, for example as carbazoles.

The above-mentioned benzenesulfonyl-carbamic acid esters or the benzenesulfonyl-thiocarbamic acid esters may contain in the alcohol component a lower-molecular alkyl radical or a phenyl radical. The same applies to the R^1 -substituted carbamic acid esters or the corresponding thiocarbamic acid esters.

As carbamic acid halides there are suitable, above all, the chlorides.

The benzenesulfonyl-ureas used as starting substances for the process of the invention may be unsubstituted, mono- or di-substituted at the urea nitrogen atom which is not attached to the sulfonyl group. Since these substituents are split off during the reaction with amines, their nature can vary within wide limits. Instead of benzenesulfonyl-ureas substituted by an alkyl, aryl, acyl or heterocyclic radical, there can likewise be used the bis-(benzenesulfonyl)-ureas, which may carry a further substituent at one nitrogen atom, for example methyl. It is, for example, possible to treat such bis-(benzenesulfonyl)-ureas or N-benzene-sulfonyl-N'-acyl-ureas with amines of the formula R^1NH_2 and to heat the salts so obtained to an elevated temperature, particularly to a temperature above 100°C .

Furthermore, it is possible to start from ureas of the formula $\text{R}^1-\text{NH}-\text{CO}-\text{NH}_2$ or from such ureas which are mono- or, in particular di-substituted at the free nitrogen atom and to react these with benzenesulfonamides substituted by the grouping



Appropriate starting substances are for example, $\text{R}'-\text{NH}-\text{CO}-\text{NH}-\text{acetyl}$, $\text{R}'-\text{NH}-\text{CO}-\text{NH}-\text{NO}_2$ and $\text{R}'-\text{NH}-\text{CO}-\text{N}-(\text{phenyl})_2$, in which case the phenyl radicals may be substituted and may be linked with one another directly or by means of a bridge member such as $-\text{CH}_2-$, $-\text{NH}-$, $-\text{O}-$ or $-\text{S}-$, N'-methyl-N'-phenyl- or N',N'-dicyclohexyl-ureas as well as the corresponding carbamoyl-imidazoles or triazoles, and finally the ureas of formula $\text{R}^1-\text{NH}-\text{CO}-\text{NH}-\text{R}^1$.

Hydrolysis of the mentioned benzenesulfonyl-parabanic acids, benzenesulfonyl-isourea-ethers, benzenesulfonyl-thiourea-ethers, benzenesulfonyl-isourea-esters or benzene-sulfonyl-haloformic acid amidines is suitably carried out in an alkaline medium. Isourea-ethers and isourea-esters can also be hydrolysed successfully in an acid medium.

The sulfur atom in correspondingly substituted benzene-sulfonyl-thioureas can be replaced by an oxygen atom, in known manner, for example with the aid of oxides or salts of heavy metals or likewise by applying oxidizing agents such as hydrogen peroxide sodium peroxide or nitrous acid.

Thioureas may also be desulfurized by treating them with phosgene or phosphorus pentachloride. Chloroformic acid amidines or carbodiimides obtained as intermediate products can be converted into the benzenesulfonyl-ureas by suitable processes such, for example, as saponification or addition of water.

Correspondingly substituted benzenesulfonyl-ureas, containing in the molecule an unsaturated bond, for example

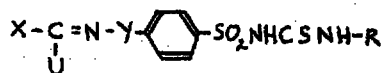


can be converted by hydrogenation, for example, with molecular hydrogen in the presence of a known hydrogenation catalyst to the benzenesulfonyl-ureas according to the present invention.

The acylation of aminoalkyl-benzenesulfonyl-ureas may be carried out either in one step, for example, by reaction of a correspondingly substituted acid halide, or it may be carried out in several steps. One example of the numerous possibilities of stepwise acylation is the reaction of aminoalkyl-benzenesulfonyl-ureas with 2-methoxy-benzoyl chloride and subsequent introduction of a halogen atom into the benzene nucleus of the benzamido group.

The sulfur atoms in correspondingly substituted thioaminoalkyl-benzenesulfonyl-ureas or thioaminoalkyl-benzenesulfonyl-thioureas can be replaced by oxygen atoms for example, with the aid of oxidizing agents such as hydrogen peroxide, sodium peroxide or other peroxide compounds.

Instead of the thioamido-alkyl-benzenesulfonyl-ureas the corresponding thioaminoalkyl-benzenesulfonyl-thiourea-ethers, isourea-ethers or -esters, thioaminoalkyl-benzenesulfonyl-parabanic acids or thioaminoalkyl-benzenesulfonyl-haloformic acid amidines can be desulfurized by treatment with oxidizing agents in an acid or alkaline medium whereby simultaneously desulfurization and hydrolysis occur thus forming the sulfonyl-urea grouping and the amidoalkyl-benzene-sulfonyl-ureas are obtained in a one-step reaction. Instead of the thioamidoalkyl-benzene-sulfonyl-thioureas, compounds of the formula



wherein U has the meaning given above, can be converted by treatment with oxidizing agents in an acid or alkaline medium by simultaneous desulfuration and hydrolysis into the amido-alkyl-benzenesulfonyl-ureas.

As regards the reaction conditions, the forms of realizing the process of the invention may, in general, vary within wide limits and can be adapted to each individual case. For example, the reactions can be carried out with the use of solvents either at room temperature or at an elevated temperature.

The hypoglycemic action of the benzenesulfonyl-urea derivatives described above could be determined by feeding them to rabbits for example in the form of sodium salt in doses of 10 mg/kg and determining the blood sugar value according to the known method by Hagedorn-Jensen or by means of an auto-analyzer over a prolonged period of time.

Thus, it was found, for example, that 10 milligrams/kilogram of N - [4 - (β - <2 - methoxy - 5 - fluoro - benzamido> - ethyl) - benzene - sulfonyl] - N' - (3,4 - dimethyl - cyclohexyl) - urea provoke, after 3 hours, a lowering of the blood sugar by 45%, which, after 24 hours still amounts to 44% and which falls to zero only after 48 hours. In the same manner, 10 milligrams of N - [4 - (β - <2 - methoxy - 5 - chloro - benzamido> - ethyl) - benzene - sulfonyl] - N' - (2,4 - dimethyl - cyclohexyl) - urea provoke after 3 hours a blood sugar lowering of 31%, which after 24 hours even amounts to 39%, and 10 mg of N - [4 - (β - <2 - methoxy - 5 - chloro - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ³ - cyclohexenyl) - urea provoke after 3 hours a lowering of the blood sugar of 22%, which, after 24 hours still amounts to 19%, whereas the known N - [4 - methyl - benzene - sulfonyl] - N' - butyl - urea, when administered to rabbits in doses of less than 25 mg/kg, does not provoke a lowering of the blood sugar level. The strong hypoglycemic action of the benzenesulfonyl-ureas of the present invention becomes more evident if the dose is further reduced. When N - [4 - (β - <2 - n - propoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethyl - cyclohexyl) - urea is administered to rabbits in a dose of 0.02 mg/kg and N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) -

benzenesulfonyl] - N' - (3,4 - dimethyl - cyclohexyl) - urea is administered to rabbits in a dose of 0.01 mg/kg, and when N - [4 - (β - <2 - methoxy - 5 - fluorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethyl - cyclohexyl) urea is administered to rabbits in a dose of 0.008 mg/kg, a distinct lowering of the blood sugar can still be observed.

Furthermore, it was found, that 10 mg/kg of N - [4 - (β - <2 - ethoxy - 5 - fluoro - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea provoke after 3 hours a lowering of the blood sugar of 39%, which, after 24 hours still amounts to 28% and after 48 hours to 16%, and falls to zero only after 72 hours, that 10 mg/kg of N - [4 - (β - <2 - ethoxy - 5 - fluoro - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methyl - cyclohexyl) - urea provoke after 3 hours a lowering of the blood sugar of 32%, which, after 24 hours still amounts to 21%, and falls to zero only after 48 hours.

10 mg/kg of N - [4 - (β - <2 - methoxy - 5 - chloro - benzamido> - ethyl) - benzene - sulfonyl] - N' - (4 - chloro - cyclohexyl) - urea likewise provoke after 3 hours a lowering of the blood sugar of 25%, which, after 24 hours even amounts to 33% and after 48 hours to 25%. 10 mg/kg of N - [4 - (β - <2 - methoxy - 5 - chloro - benzamido> - ethyl) - benzenesulfonyl] - N' - (exo - tricyclo - [3,2,1,0^{2,4}] - octane - 3 - anti) - urea provoke after 3 hours a lowering of the blood sugar of 21%, which, after 24 hours amounts to 23% and after 48 hours still to 17%. 10 mg/kg of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea provoke after 3 hours a lowering of the blood sugar of 25%, which, after 24 hours amounts to 25% and after 48 hours still to 12%. When N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chloro - cyclohexyl) - urea is administered to rabbits in a dose of 0.04 mg/kg, N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chloro - cyclohexyl) - urea is administered to rabbits in a dose of 0.04 mg/kg, N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chloro - cyclohexyl) - urea is administered to rabbits in a dose of 0.02 mg/kg, N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methyl - cyclohexyl) - urea is administered in a dose of 0.1 mg/kg, N - [4 - (β - <2 - methoxy - 5 - methyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (spiro<5,5> - undecyl - <3>) - urea is administered to rabbits in a dose of 0.06 mg/kg or N - [4 - (β - <2 - methoxy - 5 - methyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methyl - cyclohexyl) - urea is administered to rabbits in a dose of 0.01 mg/kg, a distinct lowering of the blood sugar can still be observed.

As regards the toxicity of the compounds the values are within the same range as those of benzenesulfonyl-ureas, for example N - [4 - methyl - benzenesulfonyl] - N' - n - butyl urea and N - [4 - methyl - benzenesulfonyl] - N' - cyclohexyl - urea the LD₅₀ of which amounts to 2.5 or 4.8 grams/kg respectively, with oral application.

It results therefrom that the products of the invention show a very strong hypoglycemic action accompanied by a good tolerability.

The benzenesulfonyl-ureas described are preferably used for the manufacture of orally administrable pharmaceutical preparations for the lowering of the blood sugar level in the treatment of diabetes mellitus; they may be used as such or in the form of their physiologically tolerable salts or in the presence of substances which cause such salt formation. For the formation of salts there may be used, for example, alkaline agents such as alkali metal hydroxides or alkaline earth metal hydroxides, alkali metal carbonates or bicarbonates or alkaline earth metal carbonates or bicarbonates.

The pharmaceutical preparations are advantageously in the form of tablets containing the products of the present invention in admixture or conjunction with the usual pharmaceutically suitable carriers such as talc, starch, lactose, tragacanth or magnesium stearate.

A pharmaceutical preparation containing one of the aforesaid benzenesulfonyl-ureas as the active substance, for example, a tablet or a powder, with or without the aforesaid carriers, is advantageously brought into a suitable unit dosage form. The dose chosen should comply with the activity of the benzene-sulfonyl-urea used and the desired effect. Advantageously, the dosage of active ingredient per unit amounts to about 0.5 to 100 mg, preferably 2 to 10 mg, but considerably higher or lower dosage units may also be used, if desired, are divided or multiplied prior to their administration.

The following Examples serve to illustrate the invention, but they are not intended to limit it thereto.

EXAMPLE 1

N-[4-(β -<2-methoxy-5-chlorobenzamido>-ethyl)-benzenesulfonyl]-
N'-(3-methoxy-4-methylcyclohexyl)-urea

- 4.2 g of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methyl - urethane (melting point 189—191°C) are suspended in 50 ml of dioxane which dissolved after addition of 2 g of 3 - methoxy - 4 - methyl - cyclohexyl - amine - acetate (melting point 134—136°C) (obtained by hydrogenation of the nucleus of 3 - methoxy - 4 - methylaniline in the presence of a Co_2O_3 catalyst at 260°C and under a pressure of 240 atmospheres H_2) and heated for about 1 hour to 110°C, in which process the methanol which has formed during the reaction is distilled off. After cooling water is added and the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea precipitates in crystalline form and it is recrystallized from methanol (melting point 179—181°C). In analogous manner, there is obtained:
- from
N - [4 - (β - <3 - trifluoromethylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 178—180°C)
N - [4 - (β - <3 - trifluoromethylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 159—161°C (from methanol);
from
N - [4 - (β - <3,4 - dichlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 198—200°C)
N - [4 - (β - <3,4 - dichlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 190—191°C (from methanol);
from
N - [4 - (β - <3 - benzyloxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 163—164°C)
N - [4 - (β - <3 - benzyloxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methyl - cyclohexyl) - urea, melting point 177—178°C (from methanol);
from
N - [4 - (β - <3 - ethoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 163—165°C)
N - [4 - (β - <3 - ethoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 154—156°C (from methanol);
from
N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 174—176°C)
N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 184—185°C (from methanol);
from
N - [4 - (β - <2 - methoxy - 4 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 178—180°C)
N - [4 - (β - <2 - methoxy - 4 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 191—193°C (from methanol);
from
N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane, (melting point 175—177°C)
N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 177—179°C (from methanol/dimethylformamide);
from
N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - methylurethane, (melting point 197—199°C)
N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 181—183°C (from methanol/dimethylformamide);
from
N - [4 - (β - <3,5 - dimethylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 223—225°C)
N - [4 - (β - <3,5 - dimethylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 181—183°C (from methanol);
from

- 5 N - [4 - (β - <2 - allyloxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 167—169°C)
 5 N - [4 - (β - <2 - allyloxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 146—148°C (from methanol);
 10 from
 10 N - [4 - (β - <2 - ethoxy - 5 - fluorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 193—195°C)
 10 N - [4 - (β - <2 - ethoxy - 5 - fluorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 173—174°C (from methanol);
 15 from
 15 N - [4 - (β - <2 - ethoxy - 4 - trifluoromethylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 166—168°C)
 15 N - [4 - (β - <2 - ethoxy - 4 - trifluoromethylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 171—173°C (from methanol);
 20 from
 20 N - [4 - (β - tetraline (2) - carbamido) - ethyl] - benzenesulfonyl - methylurethane (melting point 176°C)
 20 N - [4 - (β - tetraline - (2) - carbamidoethyl) - benzenesulfonyl] - N' - (3 - ethoxy - 4 - methylcyclohexyl) - urea, melting point 138°C (from methanol/water).

EXAMPLE 2

- 25 N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - ethoxy - 4 - methylcyclohexyl) - urea
 25 4 g of N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 175—177°C) are suspended in 75 ml of dioxane and 1.7 g of 3 - ethoxy - 4 - methylcyclohexylamino (boiling at 80°C under a pressure of 10 mm of mercury, obtained by hydrogenation of the nucleus of 3 - ethoxy - 4 - methylaniline in the presence of a CO₂O₃ catalyst at 260°C and 250 atmospheres H₂) are added. The whole is heated for 1 hour to 110°C. Then the N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - ethoxy - 4 - methylcyclohexyl) - urea is precipitated by means of water. The crystals melt after recrystallization from methanol at 172—174°C.
 30 In analogous manner, there is obtained:
 35 from
 35 N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 173—175°C)
 40 N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - ethoxy - 4 - methylcyclohexyl) - urea, melting point 178—180°C);
 40 from
 45 N - [4 - (β - <3 - methoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 226—228°C)
 45 N - [4 - (β - <3 - methoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (3 - ethoxy - 4 - methylcyclohexyl) - urea, melting point 157—159°C (from methanol);
 50 from
 50 N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 174—176°C)
 50 N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - ethoxy - 4 - methylcyclohexyl) - urea, melting point 168—169°C (from methanol);
 55 from
 55 N - [4 - (β - <2 - n - butoxybenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 160—162°C)
 55 N - [4 - (β - <2 - n - butoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - ethoxy - 4 - methylcyclohexyl) - urea, melting point 140—142°C (from methanol);
 60 from
 60 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 189—191°C)
 60 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - ethoxy - 4 - methylcyclohexyl) - urea, melting point 173—175°C (from methanol);
 60 from

	N - [4 - (β - <2 - methoxy - 5 - benzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 197—199°C)	
5	N - [4 - (β - <2 - methoxy - 5 - bromo - benzamido> - ethyl) - benzenesulfonyl] - N' - (3 - ethoxy - 4 - methylcyclohexyl) - urea, melting point 178—180°C (from methanol); from	5
	N - [4 - (β - <3,5 - dimethylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 223—225°C)	
10	N - [4 - (β - <3,5 - dimethylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - ethoxy - 4 - methylcyclohexyl) - urea, melting point 190—192°C (from methanol); from	10
	N - [4 - (β - <2 - ethoxy - 5 - acetylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 164—166°C)	
15	N - [4 - (β - <2 - ethoxy - 5 - acetylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - ethoxy - 4 - methylcyclohexyl) - urea, melting point 155—157°C (from methanol); from	15
	N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane, (melting point 173—175°C)	
20	N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (spiro <5,5> - undecyl - <3>) - urea, melting point 211—212°C (from methanol/dimethylformamide); from	20
	N - [4 - (β - <3 - methoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 226—228°C)	
25	N - [4 - (β - <3 - methoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - spiro <5,5> - undecyl - <3>) - urea, melting point 182—183°C (from methanol); from	25
	N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 175—177°C)	
30	N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (spiro - <5,5> - undecyl - <3>) - urea, melting point 172—173°C (from methanol); from	30
	N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 197—199°C)	
35	N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - N' - (spiro - <5,5> - undecyl - <3>) - urea, melting point 194—196°C (from methanol/dimethylformamide); from	35
	N - [4 - (β - <2 - phenoxybenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 167—169°C)	
45	N - [4 - (β - <2 - phenoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (spiro - <5,5> - undecyl - <3>) - urea, melting point 166—167°C (from methanol); from	45
	N - [4 - (β - <2 - methoxy - 4 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 178—180°C)	
50	N - [4 - (β - <2 - methoxy - 4 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (spiro - <5,5> - undecyl - <3>) - urea, melting point 213—215°C (from methanol/dimethylformamide); from	50
	N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 175—177°C)	
55	N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - 4 - methoxycyclohexyl) - urea, melting point 110—112°C (from methanol); from	55
	N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 197—199°C)	
60	N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - 4 - methoxycyclohexyl) - urea, melting point 113°C (decomposition) (from methanol); from	60

- 5 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 189—191°C)
 5 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - 4 - methoxycyclohexyl) - urea, melting point 112—114°C (decomposition) (from methanol);
 10 N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methyl - urethane (melting point 173—185°C)
 10 N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methyl - 4 - methoxycyclohexyl) - urea, melting point 166—168°C (from methanol).

EXAMPLE 3

- 15 N - [4 - (β - <3 - methoxy-methoxythienyl-2-carbonamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy-4-methylcyclohexyl) - urea
 15 5 g of 4 - (β - <3 - methoxy-methoxythienyl-2-carbonamido> - ethyl) - benzenesulfonamide (melting point 160—162°C) are dissolved in 7 ml of 2N sodium hydroxide solution and 50 ml of acetone and 2.4 g of 3 - methoxy - 4 - methylcyclohexyl - isocyanate (boiling at 90°C under a pressure of 10 mm of mercury) are added dropwise at 0—5°C. Then stirring is continued for 2 hours, then the whole is diluted with water, and any undissolved matter is filtered off, and the filtrate is acidified with dilute hydrochloric acid. The N - [4 - (β - <3 - methoxy - methoxy - thiophen - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methyl - cyclohexyl) - urea precipitating in crystalline form melts at 125—127°C after recrystallization from methanol.
 20 In analogous manner there is obtained:
 25 from
 25 4 - (β - <4 - chlorobenzamido> - ethyl) - benzenesulfonamide (melting point 225—226°C)
 30 N - [4 - (β - <4 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy-4 - methylcyclohexyl) - urea, melting point 209—210°C (from methanol/dimethylformamide);
 30 from
 35 4 - (β - <3 - methylbenzamido> - ethyl) - benzenesulfonamide (melting point 197—199°C)
 35 N - [4 - (β - <3 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 167—169°C (from methanol);
 40 from
 40 4 - (β - <3,4 - tetramethylenethienyl - 2 - carbonamido> - ethyl) - benzenesulfonamide (melting point 173—174°C)
 40 N - [4 - (β - <3,4 - tetramethylene - thienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy-4 - methylcyclohexyl) - urea, melting point 187—188°C (from methanol);
 45 from
 45 4 - (β - <2 - methoxy - 5 - phenylbenzamido> - ethyl) - benzenesulfonamide (melting point 213—214°C)
 45 N - [4 - (β - <2 - methoxy - 5 - phenylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 143—145°C (from methanol);
 50 from
 50 4 - (β - <2 - phenoxybenzamido> - ethyl) - benzenesulfonamide (melting point 187—188°C)
 50 N - [4 - (β - <2 - phenoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 170—172°C (from methanol);
 55 from
 55 4 - (β - <2 - methoxy - 5 - acetylbenzamido> - ethyl) - benzenesulfonamide (melting point 206—208°C)
 55 N - [4 - (β - <2 - methoxy - 5 - acetylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea, melting point 174—176°C (from methanol/dimethylformamide);

EXAMPLE 4

- 65 N - [4 - (β - <2 - methoxy-5-chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (spiro-<5,5>-undecyl-<3>) - urea
 60 A mixture of 10.3 g of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - urea, 300 ml of toluene, 30 ml of glycol-monomethyl ether,

1.65 g of glacial acetic acid and 4.2 g of spiro <5,5> - undecyl - (3) - amine (boiling at 120—122°C under a pressure of 10mm of mercury) are heated under reflux for 5 hours. Then the whole is concentrated in vacuo, the residue is treated with alcohol and the crystals obtained of the

N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (spiro - <5,5> - undecyl - <3>) - urea are recrystallized from methanol (melting point 190°C).

In analogous manner there is obtained:

from

N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - urea (melting point 183—185°C)

N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - spiro - <5,5> - undecyl - <3>) - urea, melting point 207—209°C (from methanol/dimethylformamide);

EXAMPLE 5

N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] -

N' - (3 - methoxy - 4 - methylcyclohexyl) - urea

3.9 g of 4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl - urea and 6.7 g of N - N - diphenyl - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea (melting point 125—126°C) are heated to 110°C for 45 minutes in 100 ml of dimethylformamide. Then the whole is cooled, poured into water and ammonia of 1% strength is added. Then it is filtered off, the filtrate is acidified and the precipitate obtained is once more purified over ammonia/hydrochloric acid. The N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea which precipitates in crystalline form melts at 179—181°C after recrystallization from methanol.

EXAMPLE 6

N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] -

N' - (3 - methoxy - 4 - methylcyclohexyl) - urea

8.2 g of N - [4 - (β - acetamidoethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea (melting point 151—153°C) are heated under reflux for 2 hours with a solution of 1.6 g of sodium hydroxide in 30 ml of water. Then the whole is cooled at room temperature, 20 ml of acetone are added and 1.2 g of glacial acetic acid, and 4.1 g of 2 - methoxy - 5 - chloro - benzoyl - chloride are added in portions. After stirring for 2 hours at room temperature the whole is filtered off with suction, the precipitate is treated with a solution of bicarbonate and then it is precipitated from dilute ammonia/hydrochloric acid. The N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea melts at 179—180°C after recrystallization from methanol/dimethylformamide.

EXAMPLE 7

N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] -

N' - (4 - chlorocyclohexyl) - urea

8.5 g of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - methylurethane (melting point 189—191°C) are suspended in 100 ml of dioxane and 2.8 g of 4 - chlorocyclohexylamine (boiling point at 82—84°C under a pressure of 7 mm of mercury obtained by reaction of 4 - aminocyclohexanol with phosphorus pentachloride) are added. The reaction mixture is heated to 110°C for 1 hour, the methanol formed during the reaction is distilled off, after cooling, water is added, which leads to the precipitation of the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea which has formed. After recrystallization from methanol/dimethylformamide it melts at 177—178°C.

In analogous manner there is obtained:

N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 194—195°C (from methanol/dimethylformamide)

from

N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 173—175°C)

N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 179—180°C (from methanol);

from

	N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - methyl - urethane (melting point 174—176°C)	
	N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea, melting point 157—158°C (from methanol) and	
5	N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 198—199°C (from methanol/dimethylformamide);	5
	from	
10	N - [4 - (β - <2 - n - propoxybenzamido> - ethyl) - benzenesulfonyl] - methyl - urethane (melting point 159—161°C)	10
	N - [4 - (β - <2 - n - propoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 100—102°C (from methanol);	
	from	
15	N - [4 - (β - <2 - n - butoxybenzamido> - ethyl) - benzenesulfonyl] - methyl - urethane (melting point 160—162°C)	15
	N - [4 - (β - <2 - n - butoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 131—133°C (from methanol);	
	from	
20	N - [4 - (β - <2 - methoxy - 4 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 178—180°C)	20
	N - [4 - (β - <2 - methoxy - 4 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea, melting point 181—182°C (from methanol);	
	from	
25	N - [4 - (β - <2 - ethoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 203—205°C)	25
	N - [4 - (β - <2 - ethoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 162—164°C (from methanol);	
	from	
30	N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 197—199°C)	30
	N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea, melting point 180—182°C (from methanol) and	
	N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 198—199°C (from methanol/dimethylformamide);	35
	from	
	N - [4 - (β - <2 - ethoxy - 5 - fluorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 193—195°C)	
40	N - [4 - (β - <2 - ethoxy - 5 - fluorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea, melting point 159—161°C (from methanol/dimethylformamide);	40
	from	
	N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 175—177°C)	
45	N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea, melting point 110—112°C (from methanol) and	45
	N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 206—207°C (from methanol/dimethylformamide);	
	from	
50	N - [4 - (β - <2,5 - dimethoxybenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 173—175°C)	50
	N - [4 - (β - <2,5 - dimethoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 143—145°C (from methanol);	
	from	
55	N - [4 - (β - <3,5 - dimethylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 223—225°C)	55
	N - [4 - (β - <3,5 - dimethylbenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea, melting point 179—181°C (from methanol) and	
60	N - [4 - (β - <3,5 - dimethylbenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 202—204°C (from methanol);	60
	from	
	N - [4 - (β - <2 - phenoxybenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 167—169°C)	

- 25
- N - [4 - (β - <2 - phenoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chloro - cyclohexyl) - urea, melting point 147—149°C (from methanol);
from
- 5 N - [4 - (β - <3 - methoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 226—228°C) 5
N - [4 - (β - <3 - methoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 200—201°C (from methanol);
from
- 10 N - [4 - (β - benzamido - ethyl) - benzenesulfonyl] - methylurethane (melting point 185—187°C) 10
N - [4 - (β - benzamido - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 186—187°C (from methanol);
from
- 15 N - [4 - (β - <3 - methylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 200—202°C) 15
N - [4 - (β - <3 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 179—181°C (from methanol);
from
- 20 N - [4 - (β - <3 - trifluoromethylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 178—180°C) 20
N - [4 - (β - <3 - trifluoromethylbenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 177—179°C (from methanol);
from
- 25 N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 173—175°C) 25
N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea, melting point 173—175°C (from methanol);
from
- 30 N - [4 - (β - <3 - methoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 226—228°C) 30
N - [4 - (β - <3 - methoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea, melting point 196—197°C (from methanol/dimethylformamide);
from
- 35 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 189—191°C) 35
N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - chlorocyclohexyl) - urea, melting point 144—146°C (from methanol/dimethylformamide);
from
- 40 N - [4 - (γ - <2 - methoxy - 5 - chlorobenzamido> - propyl) - benzenesulfonyl] - methylurethane (melting point 160°C) 40
N - [4 - (γ - <2 - methoxy - 5 - chlorobenzamido> - propyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 93° (decomposition) from methanol/water);
from
- 45 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - propyl) - benzenesulfonyl] - methylurethane (melting point 197°C) 45
N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - propyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 78°C (decomposition) (from methanol/water);
from
- 50 N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 173—175°C) 50
N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - chlorocyclohexyl) - urea, melting point 151—153°C (from methanol);
from
- 55 N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 175—177°C) 55
N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3 - chlorocyclohexyl) - urea, melting point 146—148°C (from methanol);
from
- 60 N - [4 - <3 - ethoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 163—165°C) 60

N - [4 - <3 - ethoxythienyl - 2 - carbonamido> - ethyl] - benzenesulfonyl] -
N' - (2 - chlorocyclohexyl) - urea, melting point 176—177°C (from methanol);
from

5 N - [4 - (β - <2 - allyloxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] -
methylurethane (melting point 167—169°C) 5

N - [4 - (β - <2 - allyloxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] -
N' - (2 - chlorocyclohexyl) - urea, melting point 145—147°C (from methanol);

EXAMPLE 8

10 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] -
N' - (4 - chlorocyclohexyl) - urea 10

4.26 g of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene-
sulfonyl - methyl - urethane are heated for 1 1/2 hours in a reflux condenser in 100 ml.
dioxane with 2 g of 4-chlorocyclohexylamine-acetate. After addition of water and re-
crystallization of the precipitating product from methanol/dimethylformamide there is
15 obtained in good yield the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - 15
ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea melting at 177—178°C.

EXAMPLE 9

20 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] -
N' - (2 - chlorocyclohexyl) - urea 20

A mixture of 10.3 g of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> -
ethyl) - benzenesulfonyl] - ethyl - benzenesulfonyl] - urea (melting point 171—173°C),
300 ml of toluene, 30 ml of glycolmonomethyl-ether, 1.65 g of glacial acetic acid and
3.3 g of 2 - chloro - cyclohexylamine are heated under reflux for 5 hours. Then the
whole is concentrated in vacuo and the residue is treated with alcohol. The N - [4 -
25 (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - 25
chlorocyclohexyl) - urea obtained as crude product melts at 194—195°C after recrystallization from methanol-dimethylformamide.

EXAMPLE 10

30 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] -
N' - (4 - chlorocyclohexyl) - urea 30

3.9 g of 4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesul-
fonamide sodium, 6.5 g of N,N - diphenyl - N' - (4 - chlorocyclohexyl) - urea (melting
point 115—116°C) and 100 ml dimethyl formamide are heated to 110°C for 45 min-
utes. Then the whole is cooled, poured into water and ammonia of 1% strength is
35 added. Then the whole is filtered, the filtrate is acidified and the precipitate obtained is 35
purified once more over ammonia/hydrochloric acid. The N - [4 - (β - <2 - methoxy -
5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea
precipitating in crystalline form melts at 178—179°C after recrystallization from
methanol/dimethylformamide.

EXAMPLE 11

40 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] -
N' - (4 - chlorocyclohexyl) - urea 40

7.8 g of N - [4 - (β - acetoamido - ethyl) - benzenesulfonyl] - N' - (4 - chloro-
cyclohexyl) - urea (melting point 151—153°C) are heated under reflux for 2 hours
45 with 1.6 g of sodium hydroxide and 30 ml of water. Then the whole is cooled to room 45
temperature, 20 ml of acetone are added and 1.2 g of glacial acetic acid, and 4.1 g of
2 - methoxy - 5 - chlorobenzoylchloride are added in portions and stirring is continued
for 1 hour. The precipitate is filtered off with suction, stirred with bicarbonate solution
and recrystallized from methanol/dimethylformamide. The N - [4 - (β - <2 - meth-
oxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) -
50 urea obtained melts at 178—179°C. 50

EXAMPLE 12

55 N - [4 - (β - <2 - methoxy - 4 - chlorobenzamido> - ethyl) - benzenesulfonyl] -
N' - (2 - chlorocyclohexyl) - urea 55

5 g of 4 - (β - <2 - methoxy - 4 - chlorobenzamido> - ethyl) - benzenesulfon-
amide (melting point 185—186°C) are dissolved in 7 ml of 2N sodium hydroxide solu-
tion and 50 ml of acetone and 2.3 g of 2-chlorocyclohexyl-isocyanate are added drop-
wise while stirring at 0—5°C. Then stirring is continued for 2 hours, the whole is dilu-
ted with water and methanol, and any undissolved matter is filtered off and the filtrate
60 is acidified with hydrochloric acid. The N - [4 - (β - <2 - methoxy - 4 - chlorobenz- 60

amido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea precipitating, melts at 174—176°C after recrystallization from methanol.

In analogous manner there is obtained:

- from
5 4 - (β - |<4 - chlorobenzamido> - ethyl) - benzenesulfonamide (melting point 225—226°C) 5
N - [4 - (β - |<4 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 180—181°C (from methanol);
from
10 4 - (β - |<2 - ethoxybenzamido> - ethyl) - benzenesulfonamide (melting point 148—150°C) 10
N - [4 - (β - |<2 - ethoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 147—148°C (from methanol);
from
15 4 - (β - |<3,5 - dimethylthienyl - 2 - carbonamido> - ethyl) - benzene - sulfonamide (melting point 176—177°C) 15
N - [4 - (β - |<3,5 - dimethylthienyl - 2 - carbonamido> - ethyl) - benzene - sulfonyl] - N' - (2 - chlorocyclohexyl) - urea, melting point 177—179°C (from methanol);

EXAMPLE 13

- 20 N-[4-(β-<2-methoxy-5-chlorobenzamido>-ethyl)-benzenesulfonyl]-N'-(4-chlorocyclohexyl)-urea 20
a) 2.3 g of 4-chlorocyclohexyl-parabanic acid (melting point 222—223°C) are suspended in 50 ml benzene and heated under reflux for 2 hours with 3.9 g of 4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfochloride and 1 g of triethylamine. The solvent is decanted, the remaining oil is treated with water and the undissolvable residue is recrystallized from methanol. The 1 - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - 3 - (4 - chlorocyclohexyl) - parabanic acid melts at 179—181°C. 25
b) 0.9 g of the above-mentioned compound is heated in a vapor bath for 45 minutes in 5 ml of dioxane and 10 ml of 1N sodium hydroxide solution. Then water is added, acidified and recrystallized from methanol. There is obtained the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - chlorocyclohexyl) - urea melting at 179—181°C. 30

EXAMPLE 14

- 35 N-[4-(β-<2-methoxy-5-chlorobenzamido>-ethyl)-benzenesulfonyl]-N'-2-chlorocyclohexyl urea 35
a) 1 g of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene-sulfonyl] - N' - 2 - chlorocyclohexyl - thiourea (melting point 173—175°C) is dissolved in 100 ml of methanol to which 10 ml of dioxane are added. 1.1 g of mercury peroxide are added and stirring is continued for 3 hours at 50—60°C. After filtration from the mercury sulfide, the whole is concentrated in vacuo. The N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - 2 - chlorocyclohexyl - isourea methyl ether melts at 125—127°C after recrystallization from dilute methanol. 40
b) 0.1 g of the product obtained according to a) is suspended in 2 ml dioxane and 10 ml concentrated hydrochloric acid. Then the whole is heated for 5 minutes in a vapor bath, water is added and the precipitate is filtered off with suction and crystallized from methanol. The N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - 2 - chlorocyclohexyl - urea melts at 192—194°C. 45

EXAMPLE 15

- 50 N-[4-(β-<2-methoxy-5-chlorobenzamido>-ethyl)-benzenesulfonyl]-N'-2-chlorocyclohexyl-urea 50
0.5 of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene-sulfonyl] - N' - 2 - chlorocyclohexyl - thiourea (melting point 173—175°C) is dissolved in 30 ml 2N sodium hydroxide solution, and 10 ml of hydrogen peroxide of 30% strength are added. 55
Then the whole is heated for 20 minutes in a vapor bath, cooled and acidified. A precipitate is obtained which is filtered off with suction, and treated with highly diluted ammonia. After filtration it is acidified. The N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - 2 - chlorocyclohexyl - urea melts at 192—194°C after recrystallization from methanol. 60

EXAMPLE 16

N-[4-(β -<2-methoxy-5-chlorobenzamido>-ethyl)-benzenesulfonyl]-
N'-(exo-tricyclo[3,2,1,0^{2,4}]-octane-3-anti)-urea

5 18.5 g of 4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesul-
fonamide are dissolved in 250 ml of dioxane, 13.8 g of ground potassium carbonate 5
are added and the whole is heated under reflux for 2 hours, while stirring. Then a
solution of exotricyclo[3,2,1,0^{2,4}] - octane - 3 - anti - isocyanate is added dropwise in
benzene (obtained by thermal transposition of the corresponding acid azide) and
10 stirring is continued for 5 1/2 hours at boiling temperature. The cooled solution is
poured into water, acidified, and the desired precipitated product is filtered off with 10
suction and recrystallized twice from dioxane/water. Melting point 188—190°C (under
decomposition).

In analogous manner there is obtained:

15 N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - exotri-
cyclo - [3,2,1,0^{2,4}] octane - 3 - anti) - urea, melting at 186—188°C 15

N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] -
N' - (exotricyclo - [3,2,1,0^{2,4}] - octane - 3 - anti) - urea, melting at 175—177°C (de-
composition)

20 N - [4 - (β - <4 - chloro - benzamido> - ethyl) - benzenesulfonyl] - N' - (exotri-
cyclo - [3,2,1,0^{2,4}] - octane - 3 - anti) - urea melting at 202—204°C (decomposition). 20

EXAMPLE 17

N-[4-(β -benzamido-ethyl)-benzenesulfonyl]-N'-(4-methyl- Δ 3-
cyclohexenyl)-urea

25 7.6 g of 4 - (β - benzamido - ethyl) - benzenesulfonamide are heated for 3 hours
in a reflux condenser while stirring in 150 ml of acetone with 5 g of potassium carbonate. 25
Then 3.5 g of 4 - methyl - Δ 3 - cyclohexenyl - isocyanate (boiling point of 72—
74°C under a pressure of 12 mm of mercury prepared by decomposition of the 4 -
methyl - Δ 3 - cyclohexene carboxylic acid azide obtained in usual manner from 4 -
methyl - Δ 3 - cyclohexene - carboxylic acid) are added and stirring is continued for 8
30 hours at boiling temperature. The solvent is evaporated, and the residue is treated with
water, filtered and the filtrate is acidified. The N - [4 - (β - benzamido - ethyl) - ben- 30
zenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea filtered off with suction, is
recrystallized from dilute ethanol and melts at 195—196°C.

In analogous manner there is obtained:

35 from
4 - (β - <2 - methoxy - 5 - chloro - benzamido> - ethyl) - benzenesulfonamide (melt- 35
ing point 214—216°C)

N - [4 - (β - <2 - methoxy - 5 - chloro - benzamido> - ethyl) - benzenesulfonyl] -
N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 158—160°C;

40 from
4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonamide (melting point 178—180°C) 40

N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 -
methyl - Δ 3 - cyclohexenyl) - urea, melting point 173—175°C;

45 from
4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonamide (melting point 161— 45
163°C)

N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl -
 Δ 3 - cyclohexenyl) - urea, melting point 147—149°C;

50 from
4 - (β - <4 - chloro - benzamido> - ethyl) - benzenesulfonamide (melting point 220— 50
221°C)

N - [4 - (β - <4 - chloro - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 -
methyl - Δ 3 - cyclohexenyl) - urea, melting point 201—203°C;

55 from
4 - (β - <3 - methyl - benzamido> - ethyl) - benzenesulfonamide (melting point 187— 55
189°C)

N - [4 - (β - <3 - methyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 -
methyl - Δ 3 - cyclohexenyl) - urea, melting point 160—162°C;

60 from
4 - (β - <2 - methoxy - 4 - chloro - benzamido> - ethyl) - benzenesulfonamide (melt- 60
ing point 187—188°C)

- N - [4 - (β - <2 - methoxy - 4 - chloro - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 160—162°C;
from
4 - (β - <2,4 - dichloro - benzamido> - ethyl) - benzenesulfonamide (melting point 162—164°C) 5
- N - [4 - (β - <2,4 - dichloro - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 178—180°C;
from
4 - (β - <2 - ethoxy - benzamido> - ethyl) - benzenesulfonamide (melting point 148—150°C) 10
- N - [4 - (β - <2 - ethoxy - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 158—160°C;
from
4 - (β - <2 - allyloxy - benzamido> - ethyl) - benzenesulfonamide (melting point 129—130°C) 15
- N - [4 - (β - <2 - allyloxy - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 144—146°C;
from
4 - (β - <3 - fluoro - benzamido> - ethyl) - benzenesulfonamide (melting point 218—219°C) 20
- N - [4 - (β - <3 - fluoro - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 188—190°C;
from
4 - (β - <3 - chloro - 4 - methyl - benzamido> - ethyl) - benzenesulfonamide (melting point 184—185°C) 25
- N - [4 - (β - <3 - chloro - 4 - methyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 185—187°C;
from
4 - (β - <2,5 - dimethyl - benzamido> - ethyl) - benzenesulfonamide (melting point 139—141°C) 30
- N - [4 - (β - <2,5 - dimethyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 173—175°C
from
4 - (β - <naphthalene - 2 - carbonamido> - ethyl) - benzenesulfonamide (melting point 206—208°C) 35
- N - [4 - (β - <naphthalene - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 180—182°C;
from
4 - (β - <4 - nitro - benzamido> - ethyl) - benzenesulfonamide (melting point 182—184°C) 40
- N - [4 - (β - <4 - nitro - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 172—174°C;
from
4 - (β - <2 - methoxy - 5 - methyl - benzamido> - ethyl) - benzenesulfonamide (melting point 193—194°C) 45
- N - [4 - (β - <2 - methoxy - 5 - methyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 149—151°C;
from
4 - (β - <2 - ethoxy - 5 - methyl - benzamido> - ethyl) - benzenesulfonamide (melting point 151—153°C) 50
- N - [4 - (β - <2 - ethoxy - 5 - methyl - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea, melting point 158—159°C.

EXAMPLE 18

- N-[4-(β -<2-methoxy-4-chloro-benzamido>-ethyl)-benzenesulfonyl]-
N'-(4-methyl- Δ 3-cyclohexenyl)-urea 55
- 4.2 g of N - [4 - (β - <2 - methoxy - 4 - chloro - benzamido> - ethyl) - benzene-sulfonyl] - methyl - urethane (melting point 178—180°C) are heated to 110°C while stirring, in 50 ml dioxane with 4 - methyl - Δ 3 - cyclohexenylamine (boiling point at 50°C under a pressure of 10 mm of mercury, prepared from 4 - methyl - Δ 3 - cyclohexenyl - isocyanate by saponification with acetic acid of 50% strength); during this process methanol which has formed is distilled off. Then dioxane is evaporated to a large extent under reduced pressure and water is added to the residue. The product which has precipitated is filtered off with suction and recrystallized from dilute ethanol. 60

The N - [4 - (β - <2 - methoxy - 4 - chloro - benzamido> - ethyl) - benzenesulfonyl] - N' - (4 - methyl - Δ 3 - cyclohexenyl) - urea melts at 160—162°C.

EXAMPLE 19

N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (exo-tricyclo[3,2,1,0^{2,4}]octane-3-anti)-urea

18.5 g of 4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonamide are dissolved in 250 ml dioxane, then 13.8 g ground potassium carbonate are added and the whole is heated for 2 hours under reflux. Then a solution of exo-tricyclo[3,2,1,0^{2,4}]octane - 3 - anti - isocyanate in benzene is added (obtained by thermal transposition of the corresponding acid azide) and stirring is continued for 5 1/2 hours at boiling temperature. The cooled solution is added to water, acidified, the desired precipitated product is filtered off with suction, and recrystallized twice from dioxane/water. Melting point 188—190°C (decomposition).

EXAMPLE 20

N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> ethyl) - benzenesulfonyl] - N' - (3,4 - dimethylcyclohexyl) - urea

5.7 g of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methyl - urethane (melting point 189—191°C) are suspended in 100 ml dioxane and 1.7 g of 3,4 - dimethylcyclohexylamine (boiling point 47°C under a pressure of 6 mm of mercury, acetate: melting point 114—115°C) are added. Then the whole is heated to 110°C for 1 1/2 hours while stirring, and the methanol which has formed during the reaction is distilled off. When adding a small amount of water the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3,4 - dimethylcyclohexyl) - urea crystallizes and melts after recrystallization from methanol at 170—171°C.

In analogous manner there is obtained:

N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 177—178°C (from methanol)

N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3,5 - dimethylcyclohexyl) - urea, melting point 193°C (from methanol/dimethylformamide) and

N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - diethylcyclohexyl) - urea, melting point 174—175°C (from methanol); from

N - [4 - (β - <2 - ethoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 203—204°C)

N - [4 - (β - <2 - ethoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - diethylcyclohexyl) - urea, melting point 136—138°C (from methanol); from

N - [4 - (β - <2 - allyloxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 167—168°C)

N - [4 - (β - <2 - allyloxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3,4 - dimethylcyclohexyl) - urea, melting point 158—160°C (from methanol) and

N - [4 - (β - <2 - allyloxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 156—158°C (from methanol); from

N - [4 - (β - <2 - methoxy - 5 - fluorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 171—173°C)

N - [4 - (β - <2 - methoxy - 5 - fluorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 175—176°C (from methanol)

N - [4 - (β - <2 - methoxy - 5 - fluorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3,4 - dimethylcyclohexyl) - urea, melting point 180—182°C (from methanol)

N - [4 - (β - <2 - methoxy - 5 - fluorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 196—197°C (from methanol); from

N - [4 - (β - <2 - ethoxy - 5 - fluorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 193—195°C)

N - [4 - (β - <2 - ethoxy - 5 - fluorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 167—168°C; from

N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 197—199°C)

	N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 204—205°C (from methanol/dimethylformamide)	
5	N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - N - (3,4 - dimethylcyclohexyl) - urea, melting point 166—168°C (from methanol) and N - [4 - (β - <2 - methoxy - 5 - bromobenzamido> - ethyl) - benzenesulfonyl] - N' - (3,5 - dimethylcyclohexyl) - urea, melting point 202—204°C (from methanol/dimethylformamide);	5
10	from N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 175—177°C) N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 164—166°C (from methanol);	10
15	from N - [4 - (β - <2,5 - dimethoxybenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 173—175°C) N - [4 - (β - <2,5 - dimethoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (3,4 - dimethylcyclohexyl) - urea, melting point 157—159°C (from methanol)	15
20	N - [4 - (β - <2,5 - dimethoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 132—134°C (from methanol) and N - [4 - (β - <2,5 - dimethoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - diethylcyclohexyl) - urea, melting point 142—144°C (from methanol)	20
25	from N - [4 - (β - <2 - ethoxy - 5 - acetylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 164—166°C) N - [4 - (β - <2 - ethoxy - 5 - acetylbenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 138—140°C (from methanol);	25
30	from N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 174—176°C) N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 197—199°C (from methanol/dimethylformamide)	30
35	N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (3,4 - dimethylcyclohexyl) - urea, melting point 169—171°C (from methanol) N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (3,5 - dimethylcyclohexyl) - urea, melting point 179—181°C (from methanol) and N - [4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 188—189°C (from methanol/dimethylformamide);	35
40	from N - [4 - (β - <2 - propoxybenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 159—161°C) N - [4 - (β - <2 - propoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 183—184°C (from methanol);	40
45	from N - [4 - (β - <3 - methylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 200—202°C) N - [4 - (β - <3 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 170—172°C (from methanol);	45
50	from N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 173—175°C) N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (3,4 - dimethylcyclohexyl) - urea, melting point 163—165°C (from methanol)	50
55	N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 168—169°C (from methanol) and N - [4 - (β - <3 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - diethylcyclohexyl) - urea, melting point 175—176°C (from methanol);	55
60	from N - [4 - (β - <3,5 - dimethylbenzamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 223—225°C) N - [4 - (β - <3,5 - dimethylbenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 194—195°C (from methanol);	60

from

N - [4 - (β - <3 - ethoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - methylurethane (melting point 163—165°C)

5 N - [4 - (β - <3 - ethoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 181—183°C (from methanol); 5

from

N - [4 - (β - <3,4 - tetramethylenethienyl - 2 - carbonamido> - ethyl) - benzene-sulfonyl] - methylurethane (melting point 194—196°C)

10 N - [4 - (β - <3,4 - tetramethylenethienyl - 2 - carbonamido> - ethyl) - benzene-sulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 186—187°C (from methanol). 10

EXAMPLE 21

N-[4-(β -<2-methoxy-benzamido>-ethyl)-benzenesulfonyl-N'-(4,4-diethyl-cyclohexyl)-urea

15 6 g of 4 - (β - <2 - methoxybenzamido> - ethyl) - benzenesulfonamide (melting point 178—180°C) are dissolved in 9 ml of 2N sodium hydroxide solution and 40 ml of acetone and 3.3 g of 4,4 - diethyl - cyclohexyl - isocyanate [boiling point 108—110°C under a pressure of 11 mm of mercury; obtained by reaction of 4,4 - diethyl - cyclohexylamine (boiling point 95—97°C, hydrochloride: melting point 243°C) with 20 phosgene] are added dropwise while stirring at 0—5°C. Stirring is continued for 2—3 hours at room temperature, the whole is diluted with water and methanol, then the whole is filtered from the undissolved matter and the filtrate is acidified with dilute 20 hydrochloric acid. The N - [4 - (β - <2 - methoxy - benzamido> - ethyl) - benzene-sulfonyl] - N' - (4,4 - diethyl - cyclohexyl) - urea precipitating in crystalline form 25 melts after recrystallization from methanol at 186—187°C. 25

In analogous manner there is obtained:

from 4 - (β - <2 - n - butoxybenzamido> - ethyl) - benzenesulfonamide (melting point 151—152°C)

30 N - [4 - (β - <2 - n - butoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 190—191°C (from methanol/dimethyl-formamide); 30

from

35 4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonamide (melting point 197—198°C) 35

N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 191—192°C (from methanol/dimethylformamide) and

40 N - [4 - (β - <2 - methoxy - 5 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (3,5 - dimethylcyclohexyl) - urea, melting point 203—204°C (from methanol/dimethylformamide); 40

from

4 - (β - <2 - methoxy - 4 - chlorobenzamido> - ethyl) - benzenesulfonamide (melting point 187—188°C)

45 N - [4 - (β - <2 - methoxy - 4 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 186—188°C (from methanol) and 45

N - [4 - (β - <2 - methoxy - 4 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 201—203°C (from methanol);

from

50 4 - (β - <2 - ethoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonamide (melting point 168—170°C) 50

N - [4 - (β - <2 - ethoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 195—196°C (from methanol);

from

55 4 - (β - <2 - ethoxy - 5 - acetylbenzamido> - ethyl) - benzenesulfonamide (melting point 197—198°C) 55

N - [4 - (β - <2 - ethoxy - 5 - acetylbenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 168—169°C (from methanol);

from

60 4 - (β - <2 - β - methoxyethoxybenzamido> - ethyl) - benzenesulfonamide (melting point 128—130°C) 60

N - [4 - (β - <2 - β - methoxyethoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 164—165°C (from methanol) and

- N - [4 - (β - <2 - β - methoxyethoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 190—191°C (from methanol);
 from
 4 - (β - <2 - β - methoxy - ethoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonamide (melting point 161—162°C)
 5 N - [4 - (β - <2 - β - methoxy - ethoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 163—164°C (from methanol);
 from
 10 4 - (2 - methoxybenzamido - methyl) - benzenesulfonamide (melting point 190—191°C)
 N - [4 - (2 - methoxybenzamido - methyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 210—211°C (from methanol);
 from
 15 4 - (β - <2 - phenoxybenzamido> - ethyl) - benzenesulfonamide (melting point 187—188°C)
 N - [4 - (β - <2 - phenoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 167—168°C (from methanol) and
 20 N - [4 - (β - <2 - phenoxybenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 148—150°C (from methanol);
 from
 4 - (β - <3 - methylbenzamido> - ethyl) - benzenesulfonamide (melting point 187—189°C)
 25 N - [4 - (β - <3 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 178—180°C (from methanol);
 from
 4 - (β - <N - methyl - 3 - methylbenzamido> - ethyl) - benzenesulfonamide (melting point 146°C)
 30 N - [4 - (β - <N - methyl - 3 - methylbenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 141—142°C (from methanol);
 from
 4 - (β - <3,5 - dimethylbenzamido> - ethyl) - benzenesulfonamide (melting point 194—196°C)
 35 N - [4 - (β - <3,5 - dimethylbenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 202—204°C (from methanol);
 from
 4 - (β - <3 - trifluoromethylbenzamido> - ethyl) - benzenesulfonamide (melting point 145—147°C)
 40 N - [4 - (β - <3 - trifluoromethylbenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 185—187°C (from methanol) and
 N - [4 - (β - <3 - trifluoromethylbenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 169—170°C (from methanol);
 from
 4 - (β - <3 - methoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonamide (melting point 201—203°C)
 45 N - [4 - (β - <3 - methoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 175—176°C (from methanol);
 from
 4 - (β - <3 - ethoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonamide (melting point 177—179°C)
 50 N - [4 - (β - <3 - ethoxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 168—169°C (from methanol);
 from
 4 - (β - <3 - benzyloxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonamide (melting point 196—198°C)
 55 N - [4 - (β - <3 - benzyloxythienyl - 2 - carbonamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 181—182°C (from methanol/dimethylformamide).

EXAMPLE 22

- 60 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea
 8.2 g of N - [4 - (β - <2 - methoxy - 5 - chloro - benzamido> - ethyl) - benzenesulfonyl] - urea (melting point 171—173°C) are suspended in 150 ml of dioxane

and heated under reflux for 1 hour after addition of 3.75 g of 2,4 - dimethyl - cyclohexyl - amine - acetate. Then the solvent is distilled off in vacuo and water is added to the residue. The crystals obtained of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea are recrystallized from methanol/dimethylformamide and melt at 200—201°C.

EXAMPLE 23

N-[4-(β-<2-methoxy-5-chlorobenzamido>-ethyl)-benzenesulfonyl]-N'-(4,4-dimethylcyclohexyl)-urea

a) 5.6 g of 4,4 - dimethylcyclohexyl parabanic acid (melting point 182—183°C, prepared by reaction of 4,4 - dimethylcyclohexyl-urea with oxalyl chloride) are heated under reflux for 1 1/2 hours together with 9.7 g of 4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfochloride and 2.5 g of triethylamine in 100 ml benzene. Then the whole is filtered off while hot from the undissolved matter, and the crystals which are obtained while cooling the filtrate, are treated with boiling methanol in order to extract the impurities. After recrystallization from methanol/dimethylformamide/water, the 1 - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - 3 - (4,4 - dimethylcyclohexyl) - parabanic acid melts at 196—197°C. b) 0.5 g of the above-mentioned parabanic acid is heated in a vapor bath in 5 ml of dioxane and 10 ml of 1N-sodium hydroxide solution for 45 minutes. After cooling, water is added, acidified and the N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea obtained is recrystallized from methanol (melting point 177—178°C).

EXAMPLE 24

N-[4-(β-<2-methoxy-5-chloro-benzamido>-ethyl)-benzenesulfonyl]-N'-(4,4-dimethyl-cyclohexyl)-urea

1) 2.9 g of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - N' - (4,4 - dimethylcyclohexyl) - thiourea (prepared by reaction of 4 - [β - <2 - methoxy - 5 - chlorobenzamido> - ethyl] - benzenesulfonamide with 4,4-dimethyl cyclohexyl mustard oil in dioxane/acetone in the presence of potassium carbonate) melting point 175—177°C and decomposition, are dissolved in 250 ml acetone. An aqueous solution of 0.7 g sodium nitrate is added and while stirring is continued at 5°C, 15 ml of 5N acetic acid is added dropwise. After stirring for 2 1/2 hours acetone is distilled off. The residue is dissolved in dilute sodium hydroxide solution, the solution is clarified with charcoal and acidified. There is obtained a crystalline precipitate of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, which is filtered off with suction and recrystallized from dilute methanol. The substance melts at 174—176°C. 2) a) 5.38 g of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzene - sulfonyl] - N' - (4,4 - dimethylcyclohexyl) - thiourea are dissolved in 5 ml dioxane and 250 ml methanol. Then 2.16 g of mercury peroxide are added and stirring is continued for 4 hours at 60°C. The mercury sulfide formed is filtered off, and the filtrate is half concentrated and water is added. After leaving over night a crystalline precipitate has formed, which is filtered off with suction and recrystallized from dilute methanol. The N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - isoureamethylether thus obtained melts at 149—151°C.

b) 0.5 g of isourea ether obtained according to the method 2) a) are dissolved in 5 ml dioxane. After addition of 20 ml 2N sodium hydroxide the whole is heated in a vapor bath for 45 minutes. By acidifying there is obtained a crystalline precipitate of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea melting at 174—176°C after recrystallization from dilute methanol.

EXAMPLE 25

N-[4-(β-benzamido-ethyl)-benzenesulfonyl]-N'-(4,4-diethyl-cyclohexyl)-urea

a) 6.4 g of 4 - (β - benzamido - ethyl) - benzenesulfonamide sodium and 7.2 g of 4 - (β - benzamido - ethyl) - benzenesulfonyl - carbamic acid methyl ester are well mixed. The substance is introduced into an Erlenmeyer flask having a content of 300 ml so that the bottom of the flask is covered. Then the flask is put to an oil bath pre-heated to 250°C. After a few minutes the mass starts to drip, after another 5 minutes solidification can be observed.

The whole is cooled, the reaction cake is treated with about 1% of aqueous ammonia, it is filtered, and the filtrate is acidified with 2N hydrochloric acid. There is obtained a crystalline precipitate of N,N' - bis - 4 - [β - (benzamido - ethyl) - benzenesulfonyl] - urea, which is dissolved once more in dilute ammonia and which precipitates by acidification with hydrochloric acid. The substance melts after filtration with suction and recrystallization at 204°C and decomposition.

b) 3.17 g of the bis-urea, obtained according to method a) are suspended in 100 ml dioxane. 0.78 g of 4,4 - diethylcyclohexyl - amine are added while stirring and salt formation can be observed. Then the whole is heated to boiling temperature for 1 hour while stirring; after a few minutes the suspension has changed into a clear solution.

The whole is concentrated in vacuo, the residue is treated with ammonia of about 1% strength and then it is filtered. The filtrate gives by acidification a crystalline precipitate of N - [4 - (β - benzamido - ethyl) - benzenesulfonyl] - N' - (4,4 - diethyl - cyclohexyl) - urea. The substance melts after recrystallization from methanol at 199—201°C.

EXAMPLE 26

N - [4 - (γ - <2-methoxy-5-bromobenzamido> - propyl) - benzenesulfonyl] - N' - (4,4-dimethylcyclohexyl) - urea

9 g of 4 - (γ - <2 - methoxy - 5 - bromobenzamido> - propyl) - benzenesulfonamide sodium and 16 g of N,N - diphenyl - N' - (4,4 - dimethylcyclohexyl) - urea are heated for 7 hours in an oil bath at 100°C in 30 ml of dimethylformamide. Then the whole is cooled, water and alkalies are added to the reaction mixture and the diphenylamine which has formed is etherized. The aqueous phase is treated with charcoal and the filtrate is acidified. The desired sulfonyl-urea obtained is recrystallized from methanol/water and melts at 192°C.

In analogous manner there is obtained:

N - [4 - (γ - <2 - methoxy - 5 - bromobenzamido> - propyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 184°C (from methanol/water),
 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - propyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 153°C (from methanol/water)
 N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - propyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 181°C (from methanol/water)
 N - [4 - (β - naphth - <1'> - amidoethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 216°C (from methanol/water) and
 N - [4 - (β - tetralincarb - <2'> - amidoethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 167°C (from methanol/water).

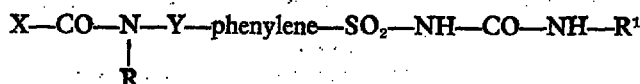
EXAMPLE 27

N - [4 - (β - <2-methoxy-5-chlorobenzamido> - α -methyl-ethyl) - benzenesulfonyl] - N' - (4,4-diethyl-cyclohexyl) - urea

9.6 g of 4 - (β - <2 - methoxy - 5 - chlorobenzamido> - α - methyl - ethyl) - benzenesulfonamide are dissolved in 250 ml of dioxane. 6.9 g of finely ground potassium carbonate are added and the whole is heated at boiling temperature for 2 hours while stirring. 4.5 g of 4,4 - diethylcyclohexyl - isocyanate are added dropwise while continuing to stir. Stirring and heating is continued for 8 hours, the whole is poured into water and acidified. The crystalline precipitate obtained is filtered off with suction and dried. The whole is dissolved in dimethylformamide, methanol is added and thus a crystalline mass is obtained of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - α - methyl - ethyl) - benzenesulfonyl] - N' - (4,4 - diethyl - cyclohexyl) - urea melting at 161—163°C.

WHAT WE CLAIM IS:—

1. Benzenesulfonyl-ureas corresponding to the general formula



in which

R represents a lower alkyl or phenyl-lower-alkyl radical, or a hydrogen atom,

R¹ represents

(a) a cyclohexyl radical containing a methyl group and an alkoxy group containing 1 or 2 carbon atoms,

(b) a chlorocyclohexyl group;

(c) a spiro-(5,5)undecyl-(3) group of the formula

The whole is cooled, the reaction cake is treated with about 1% of aqueous ammonia, it is filtered, and the filtrate is acidified with 2N hydrochloric acid. There is obtained a crystalline precipitate of N,N' - bis - 4 - [β - (benzamido - ethyl) - benzenesulfonyl] - urea, which is dissolved once more in dilute ammonia and which precipitates by acidification with hydrochloric acid. The substance melts after filtration with suction and recrystallization at 204°C and decomposition.

b) 3.17 g of the bis-urea, obtained according to method a) are suspended in 100 ml dioxane. 0.78 g of 4,4 - diethylcyclohexyl - amine are added while stirring and salt formation can be observed. Then the whole is heated to boiling temperature for 1 hour while stirring; after a few minutes the suspension has changed into a clear solution.

The whole is concentrated in vacuo, the residue is treated with ammonia of about 1% strength and then it is filtered. The filtrate gives by acidification a crystalline precipitate of N - [4 - (β - benzamido - ethyl) - benzenesulfonyl] - N' - (4,4 - diethyl - cyclohexyl) - urea. The substance melts after recrystallization from methanol at 199—201°C.

EXAMPLE 26

N - [4 - (γ - <2-methoxy-5-bromobenzamido> - propyl) - benzenesulfonyl] - N' - (4,4-dimethylcyclohexyl) - urea

9 g of 4 - (γ - <2 - methoxy - 5 - bromobenzamido> - propyl) - benzenesulfonamide sodium and 16 g of N,N - diphenyl - N' - (4,4 - dimethylcyclohexyl) - urea are heated for 7 hours in an oil bath at 100°C in 30 ml of dimethylformamide. Then the whole is cooled, water and alkalis are added to the reaction mixture and the diphenylamine which has formed is etherized. The aqueous phase is treated with charcoal and the filtrate is acidified. The desired sulfonyl-urea obtained is recrystallized from methanol/water and melts at 192°C.

In analogous manner there is obtained:

N - [4 - (γ - <2 - methoxy - 5 - bromobenzamido> - propyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 184°C (from methanol/water),
N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - propyl) - benzenesulfonyl] - N' - (4,4 - dimethylcyclohexyl) - urea, melting point 153°C (from methanol/water)
N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - propyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 181°C (from methanol/water)
N - [4 - (β - naphth - <1'> - amidoethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 216°C (from methanol/water) and
N - [4 - (β - tetralincarb - <2'> - amidoethyl) - benzenesulfonyl] - N' - (2,4 - dimethylcyclohexyl) - urea, melting point 167°C (from methanol/water).

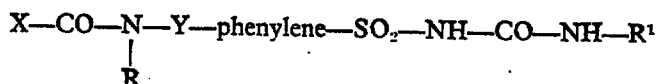
EXAMPLE 27

N - [4 - (β - <2-methoxy-5-chlorobenzamido> - α -methyl-ethyl) - benzenesulfonyl] - N' - (4,4-diethyl-cyclohexyl) - urea

9.6 g of 4 - (β - <2 - methoxy - 5 - chlorobenzamido> - α - methyl - ethyl) - benzenesulfonamide are dissolved in 250 ml of dioxane. 6.9 g of finely ground potassium carbonate are added and the whole is heated at boiling temperature for 2 hours while stirring. 4.5 g of 4,4 - diethylcyclohexyl - isocyanate are added dropwise while continuing to stir. Stirring and heating is continued for 8 hours, the whole is poured into water and acidified. The crystalline precipitate obtained is filtered off with suction and dried. The whole is dissolved in dimethylformamide, methanol is added and thus a crystalline mass is obtained of N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - α - methyl - ethyl) - benzenesulfonyl] - N' - (4,4 - diethyl - cyclohexyl) - urea melting at 161—163°C.

WHAT WE CLAIM IS:—

1. Benzenesulfonyl-ureas corresponding to the general formula



in which

R represents a lower alkyl or phenyl-lower-alkyl radical, or a hydrogen atom,

R¹ represents

(a) a cyclohexyl radical containing a methyl group and an alkoxy group containing 1 or 2 carbon atoms,

(b) a chlorocyclohexyl group,

(c) a spiro-(5,5)undecyl-(3) group of the formula





- (d) an exo-tricyclo-(3,2,1,0^{2,4}) octane group of the formula



- 5 (e) a 4-methylcyclohexenyl group, or 5
 (f) a dimethyl- or 4,4-diethylcyclohexyl group;
 X represents
 (a) a phenyl radical, carrying in any desired positions the substituents Z and Z'
 10 Z represents a hydrogen or halogen atom or a lower alkyl, lower alkenyl, lower 10
 alkoxy, lower alkenoxy, lower halogen-alkoxy, lower alkoxyalkoxy, phenyl-
 lower-alkoxy, phenyl lower alkyl, lower cycloalkoxy, phenyl, phenoxy, lower
 acyl, lower acyloxy or a benzoyl radical, or a trifluoromethyl, hydroxyl, —CN,
 or —NO₂ group,
 15 Z' represents a hydrogen or halogen atom or a lower alkyl, lower alkoxy, lower 15
 alkoxyalkoxy or lower acyloxy radical or a hydroxyl group,
 (b) a naphthyl radical which may be mono- or di-substituted by a halogen atom
 or a lower alkyl or lower alkoxy radical or a hydroxyl group,
 (c) a tetrahydronaphthyl radical or an indanyl radical,
 20 (d) a thienyl radical which may be mono- or di-substituted by substituents selec- 20
 ted from lower alkyl, phenyl-lower-alkyl, lower alkoxy, lower alkoxyalkoxy,
 lower alkenoxy, phenyl-lower-alkoxy and aryl radicals and halogen atoms,
 (e) a tetra methylene-thienyl radical or a trimethylene-thienyl radical, and
 Y represents a hydrocarbon chain of 1—3 carbon atoms,
 25 and wherein the phenylene group may be substituted by one or more substituents 25
 selected from halogen, lower alkyl or lower alkoxy.
 2. Benzenesulfonyl-ureas as claimed in claim 1, wherein R represents a hydrogen
 atom, X has the meaning given under (a) and Y represents the grouping

$$-\text{CH}_2-\text{CH}_2-$$

 30 3. Benzenesulfonyl-ureas as claimed in claim 1, wherein X and Y represent any 30
 one of the groups specifically mentioned herein.
 4. Benzenesulfonyl-ureas as claimed in any one of claims 1 to 3, wherein R'
 represents any one of the groups specifically mentioned herein.
 35 5. N - [4 - (β - <2 - methoxy - 5 - fluorobenzamido> - ethyl) - benzenesul- 35
 fonyl] - N' - (4,4 - dimethylcyclohexyl) - urea.
 6. N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesul-
 fonyl] - N' - (3,4 - dimethylcyclohexyl) - urea.
 7. N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesul-
 40 fonyl] - N' - (4 - chlorocyclohexyl) - urea.
 8. N - [4 - (β - <2 - methoxy - 5 - chlorobenzamido> - ethyl) - benzenesul- 40
 fonyl] - N' - (3 - methoxy - 4 - methylcyclohexyl) - urea.
 9. Any one of the benzenesulfonyl-ureas as claimed in claim 1 and described
 in the Examples herein, other than the compounds claimed in claims 5 to 8.
 10. Physiologically tolerable salts of any one of the compounds claimed in any
 45 one of claims 1 to 9. 45
 11. A pharmaceutical preparation for oral administration and lowering the blood
 sugar level in the treatment of diabetes mellitus, which comprises a benzenesulfonyl-
 urea compound as claimed in claim 1, or a physiologically tolerable salt thereof, in
 admixture or conjunction with a pharmaceutically suitable carrier.
 50 12. A pharmaceutical preparation for oral administration and lowering the blood 50
 sugar level in the treatment of diabetes mellitus, which comprises a compound as claimed
 in any one of claims 2 to 9, or a physiologically tolerable salt thereof, in admixture or
 conjunction with a pharmaceutically suitable carrier.
 55 13. A pharmaceutical preparation as claimed in claim 11 or claim 12, which con- 55
 tains in dosage unit form from 2 to 10 milligrams of the active ingredient.



14. A pharmaceutical preparation as claimed in any one of claims 11 to 13, which is in the form of a tablet.

15. A process for the manufacture of benzenesulfonyl-ureas as claimed in any one of claims 1 to 10, substantially as described herein.

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